

Claims

- [c1] 1. The invention of a technique for the design of changes in peptide and peptide-like sequences with specific deamidation rates using the following steps:
- (a) The determination of a table of constants for atoms or groups or groups of atoms. This table already has been made for many functional groups and can be expanded.
 - (b) The summing up of constants from the table in (a) depending on type of functional group and location in residue or residue-like structure to the right of the amide.
 - (c) The conversion of the summed constants from (b) into a deamidation rate for the primary sequence being considered.
 - (d) Where other types of secondary, tertiary or quaternary structures effect the rate, the modification of the rate derived in (c) to include these parameters.
- [c2] 2. The invention of a method to qualitatively slow down or accelerate deamidation rates by predictable amounts through addition or subtraction of atoms or groups of atoms in the vicinity of the amide without direct refer-

ence to a table of values.

- [c3] 3. The use of the techniques described in claims 1 and/or 2 to design amide structures, peptide or peptide-like structures, hormone or hormone-like structures, or protein or protein-like structures with specific modifications of deamidation rates or designed deamidation rates as a part of a pharmaceutical, industrial or other type of preparation or process.
- [c4] 4. The use of the techniques described in claims 1 and/or 2 to modify existing chemical structures either already in use in pharmaceutical or industrial applications, currently existing for potential use in these applications or not yet invented, using the techniques in claims 1 and/or 2 to either speed up or slow down deamidation rates.
- [c5] 5. The use of the techniques described in claims 1 and/or 2 to stabilize molecules for pharmaceutical, industrial, or other types of preparations or processes.
- [c6] 6. As an example of these applications the invention of stable forms of insulin with respect to deamidation at Asn(B3) of the ValAsn(B3)Gln sequence that involve:
 - (a) Addition of a methyl group to the Gln(B4) side-chain to produce the side chain $\text{CH}(\text{CH}_3)\text{CH}_2\text{CONH}_2$ – which will have a slowed deamidation rate.

(b) Addition of 2 methyl groups to the Gln(B4) side-chain to produce the side chain $C(CH_3)_2CH_2CONH_2$ – which should have a deamidation rate even slower than the structure described in (a).

(c) Other modifications using the techniques of claims 1 and 2 to modify the Gln(B4) side chain.